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10/593,145	09/18/2006	Yuichi Oku	OKUY3002/GAL	8771

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EXAMINER	
JANSSEN, SHANNON L	
ART UNIT	PAPER NUMBER
1636	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,145	OKU ET AL.	
	Examiner	Art Unit	
	SHANNON JANSSEN	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *52 and 58-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52 and 58-62* is/are rejected.

7)☒ Claim(s) *52* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *December 29, 2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 52 and 58-62 are pending in the instant application and are the subject of the Office Action below. Claim 52 was amended, claims 58-62 were added, and claims 1-14, 18, 19, 24-49, and 51 were cancelled in the amendments received January 25, 2011.

Please note: the examiner of record has changed. Please address all future correspondence to the examiner listed at the conclusion of this action.

It is noted that applicants point to the specification, [109-114, 146-150], however, [0117] appears to be more pertinent for providing support for the limitation that the nucleic acid is immobilized to the support "without passing through protein."

New Objections

Specification

The disclosure is objected to because of the following informalities: on p 81, the last line, "polyethylene resins" appears twice. Deletion of one is recommended.

Appropriate correction is required.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

Claim 52 is objected to because of the following informalities: "polystylene" and "elasmoter" in line 13 should be "polystyrene" and "elastomer," respectively. Appropriate correction is required.

Previous Rejection Withdrawn

Any rejection or objection to the claims not reiterated in the Office Action below is considered withdrawn.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52 and 58-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 52 recites "cyclic olefin copolymers and materials derived therefrom by surface modifications." However, the instant specification, [0113], states "cyclic olefin copolymers and, further, members made of these materials and subjected to surface modifications." Therefor it is unclear if with surface modifications or if the claim only encompasses cyclic olefin copolymers with surface modifications.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham **v.** John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 52, 58 and 60-62 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Elkins (US Patent 6316186, granted November 13, 2001), Fixe et al. (Functionalization of poly(methyl methacrylate) (PMMA) as a substrate for DNA microarrays, 2004, Nucleic Acids Research, Vol 32, e9, pp 1-8, published online January 12, 2004), and Chazan et al. (US Patent Application Publication 2002/0025280, published February 28, 2002).

Regarding present **claim 52**, Elkins teaches a method for analyzing analytes in a sample comprising immobilizing a plurality of nucleic acid capture agents (i.e.: N1g, g being an integer, as Elkins et al. teach 8-30 nucleotides; see claims 1-2, Figure 1) on a substrate and adding a plurality of binding agents, such as antibodies, coupled to a tail sequence that hybridizes to the capture agent on the support (i.e.: a conjugate species N2h-L1i, wherein h and i are each an integer, wherein N2 has a base sequence complementary to N1 and wherein L1 is an antibody species "capable" of binding to an antigen; see col 3, lns 45-28-53), and allowing the antibody conjugates to bind their respective capture nucleic acids (see claim 1, Figure 2) immobilized on the support (i.e.: capture zone; see entire document, particularly col 2, lns 27-64, col 3, lns 28-53claims 1-2, Figures 1-2, Examples).

Regarding present **claims 60-62**, Elkins teaches kits for analysis of analytes (see col 5, lns 53+).

While Elkins teaches a method comprising immobilizing nucleic acid species on a support as capture agents for complementary nucleic acid-antibody conjugates and analytical

kits, Elkins does not teach wherein the nucleic acid species immobilized on the support do not pass through a protein.

Regarding present **claim 52**, Fixe et al. teach nucleic acids bound to a poly(methyl methacrylate), PMMA, substrate directly through amino groups (see entire document, particularly col 2, last para, p 2, col 1, para 2, col 2, para 1, p 3, col 1, paras 2-3, Figure 1), and further teach hybridizing nucleic acids to the nucleic acids immobilized on the support (see p 5, col 1, para 2). Fixe et al. further teach the benefits of covalently binding the nucleic acids to the support:

> "These results indicate that the probes are covalently immobilized to the plastic surface and that this type of chemistry and plastic polymer can be very useful in the development of new devices for different kinds of bioassays involving heat, e.g. PCR techniques." (see p 7, col 2, para 2).
>
> The chemical reaction described in this paper to modify PMMA was simpler and faster than the procedures already described for PMMA modification. The density of immobilized and hybridized DNA to microarrays on chemically modified PMMA was similar to densities obtained on silanized glass and on PMMA chemically modified by others. Immobilized and hybridized densities of 10 and 0.75 pmol/cm2 were obtained for 2 h of immobilization (with 20 mM of spotted DNA probes) and 5 h of hybridization (with 0.2 mM of DNA target), respectively. Furthermore, the covalently immobilized oligonucleotides were stable to heat cycling suggesting that functions like PCR could be integrated in the same biochip. The ability to robustly immobilize DNA and other biomolecules on plastic polymers, presents new possibilities in the development and fabrication of specialized lab-on-a-chip systems, including both sample preparation, amplification and detection." (See p 7, col 2, para 3 through p 8, col 1).

While Elkins and Fixe et al. teach a method comprising immobilizing nucleic acid species on a support as capture agents for complementary nucleic acid-antibody conjugates, Elkins and Fixe et al. do not teach forming a substrate comprising a groove with an inlet and outlet port (i.e.: a microfluidic channel).

Regarding present **claim 52**, Chazan et al. teach a method of forming a microfluidic device comprising thermally bonding (i.e.: thermal fusion) a first substrate, comprising a groove

and multiple ports for introducing liquid (i.e.: passage inlet and passage outlet; see [0038, 0046], and part 114 in Figure 1), to a second substrate to form a microfluidic channel (i.e.: wherein the groove forms a portion of a passage upon joining the first resin member and the second resin member together and one or both have a passage inlet and a passage outlet; see [0015, 0038, 0046]), wherein the substrate is a polymeric substrate such as polydimethylsiloxane, polycarbonate, and polystyrene (see [0033, 0037]), and wherein the first and second substrates are thermally bonded at a temperature between 90 and 150° C (see [0032]), and further teach utilizing the device for, e.g., biological applications such as PCR and genotyping, and would be expected to be functional for other biological applications such as those taught by Elkins and Fixe et al. (see entire document, particularly [0033, 0038, 0046, 0061-0063]). Chazan et al. also teach wherein the microfluidic channels and passages have a depth and width of 0.1 μm and 500 μm (see [0071]).

Regarding present **claim 58**, Chazan et al. teach wherein the substrate material can be any number of polymeric materials such as polydimethylsiloxane, polycarbonate, and polystyrene (i.e.: the same; see [0033, 0036, 0037]).

Therefore it would have been obvious to one of skill in the art at the time of the invention to immobilize the nucleic acids directly to the support as taught by Fixe et al. and to utilize a microfluidic device as taught by Chazan et al. in the method of analyzing samples taught by Elkins.

One would have been motivated to do so because Fixe et al. teach the stability of the covalent binding of the nucleic acids to the support and discuss the new possibilities for

developing specialized systems (see p 8, col 2, paras1-2), and Chazan et al. teach the benefits of microfluidic devices, such as high-throughput assays and the ability to perform multiple reactions simultaneously in parallel, and the ability to precisely control temperature for biological reactions such as PCR and single nucleotide polymorphism genotyping (see [0006-0007).

One would have had a reasonable expectation for success because Fixe et al. teach successfully immobilizing nucleic acids directly to the support and that the resulting bond was heat stable, Chazan et al. teach successfully manufacturing microfluidic devices for such as PCR and single nucleotide polymorphism genotyping, which are biological assays, and Elkins teaches successfully assaying samples by utilizing nucleic acid capture agents.

Therefor the teachings of Elkins, Fixe et al., and Chazan et al. renders the present invention prima facie obvious.

In addition, it would have been obvious to one skilled in the art to substitute one known element (i.e.: binding the nucleic acid directly to the support taught by Fixe et al. and a microfluidic device as the support as taught by Chazan et al.) for another known element (i.e.: binding through a biotin linkage and array support taught by Elkins) using known methods (i.e.: the methods taught by all the cited references) with no change in their respective functions, and the substitution would have yielded the predictable results of a microfluidic device comprising nucleic acids bound directly to the substrate to one of ordinary skill in the art at the time of the invention. See KSR International Co. v. Teleflex Inc., USPQ2d 1385 (U.S. 2007).

Claims 52 and 58-62 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Elkins (US Patent 6316186, granted November 13, 2001), Fixe et al. (Functionalization of

poly(methyl methacrylate) (PMMA) as a substrate for DNA microarrays, 2004, Nucleic Acids Research, Vol 32, e9, pp 1-8, published online January 12, 2004), Yamagata et al. (EP 1371990, published November 12, 2003, provided by applicants in IDS), and Chazan et al. (US Patent Application Publication 2002/0025280, published February 28, 2002).

Regarding present **claim 52**, Elkins teaches a method for analyzing analytes in a sample comprising immobilizing a plurality of nucleic acid capture agents (i.e.: N1g, g being an integer, as Elkins et al. teach 8-30 nucleotides; see claims 1-2, Figure 1) on a substrate and adding a plurality of binding agents, such as antibodies, coupled to a tail sequence that hybridizes to the capture agent on the support (i.e.: a conjugate species N2h-L1i, wherein h and i are each an integer, wherein N2 has a base sequence complementary to N1 and wherein L1 is an antibody species "capable" of binding to an antigen; see col 3, lns 45-28-53), and allowing the antibody conjugates to bind their respective capture nucleic acids (see claim 1, Figure 2) immobilized on the support (i.e.: capture zone; see entire document, particularly col 2, lns 27-64, col 3, lns 28-53claims 1-2, Figures 1-2, Examples).

Regarding present **claims 60-62**, Elkins teaches kits for analysis of analytes (see col 5, lns 53+).

While Elkins teaches a method comprising immobilizing nucleic acid species on a support as capture agents for complementary nucleic acid-antibody conjugates and analytical kits, Elkins does not teach wherein the nucleic acid species immobilized on the support do not pass through a protein.

Regarding present **claim 52**, Fixe et al. teach nucleic acids bound to a poly(methyl methacrylate), PMMA, substrate directly through amino groups (see entire document,

particularly col 2, last para, p 2, col 1, para 2, col 2, para 1, p 3, col 1, paras 2-3, Figure 1), and further teach hybridizing nucleic acids to the nucleic acids immobilized on the support (see p 5, col 1, para 2). Fixe et al. further teach the benefits of covalently binding the nucleic acids to the support:

> "These results indicate that the probes are covalently immobilized to the plastic surface and that this type of chemistry and plastic polymer can be very useful in the development of new devices for different kinds of bioassays involving heat, e.g. PCR techniques." (see p 7, col 2, para 2).
>
> The chemical reaction described in this paper to modify PMMA was simpler and faster than the procedures already described for PMMA modification. The density of immobilized and hybridized DNA to microarrays on chemically modified PMMA was similar to densities obtained on silanized glass and on PMMA chemically modified by others. Immobilized and hybridized densities of 10 and 0.75 pmol/cm2 were obtained for 2 h of immobilization (with 20 mM of spotted DNA probes) and 5 h of hybridization (with 0.2 mM of DNA target), respectively. Furthermore, the covalently immobilized oligonucleotides were stable to heat cycling suggesting that functions like PCR could be integrated in the same biochip. The ability to robustly immobilize DNA and other biomolecules on plastic polymers, presents new possibilities in the development and fabrication of specialized lab-on-a-chip systems, including both sample preparation, amplification and detection." (See p 7, col 2, para 3 through p 8, col 1).

While Elkins and Fixe et al. teach a method comprising immobilizing nucleic acid species on a support as capture agents for complementary nucleic acid-antibody conjugates, Elkins and Fixe et al. do not teach forming a substrate comprising a groove with an inlet and outlet port (i.e.: a microfluidic channel).

Regarding present **claim 52**, Yamagata et al. teach a method of forming microfluidic channels for assaying samples comprising immobilizing a plurality of biomolecules on the surface of a substrate, such as a PMMA or polycarbonate substrate, and bonding a second substrate, such as a PMMA or polycarbonate substrate, comprising a plurality of channels and an inlet and outlet port to the first substrate, and injecting a reaction sample into the inlet ports so

that it flows through the channels (see entire document, particularly [0027-0029, 0031-0035], Figures, claims 1-13). Yamagata et al. further teach wherein bonding the first and second substrates can be accomplished by heating (see [0034]).

Regarding present **claims 58-59**, Yamagata et al. teach wherein the first and second substrate materials can be any number of polymeric materials such as PMMA, polycarbonate, and polyethylene (i.e.: the same or different; see [0027, 0033]).

While Elkins, Fixe et al., and Yamagata et al. teach a method comprising immobilizing nucleic acid species on a support as capture agents for complementary nucleic acid-antibody conjugates and bonding a second substrate comprising grooves to the support comprising nucleic acids to form microfluidic channels, Elkins, Fixe et al., and Yamagata et al. do not teach a temperature of heating to bond the substrates or a size of microfluidic channels.

Regarding present **claim 52**, Chazan et al. teach a method of forming a microfluidic device comprising thermally bonding (i.e.: thermal fusion) a first substrate, comprising a groove and multiple ports for introducing liquid (i.e.: passage inlet and passage outlet; see [0038, 0046], and part 114 in Figure 1), to a second substrate to form a microfluidic channel (i.e.: wherein the groove forms a portion of a passage upon joining the first resin member and the second resin member together and one or both have a passage inlet and a passage outlet; see [0015, 0038, 0046]), wherein the substrate is a polymeric substrate such as polydimethylsiloxane, polycarbonate, and polystyrene (see [0033, 0037]), and wherein the first and second substrates are thermally bonded at a temperature between 90 and 150° C (see [0032]), and further teach utilizing the device for, e.g., biological applications such as PCR and genotyping, and would be expected to be functional for other biological applications such as those taught by Elkins and

Fixe et al. (see entire document, particularly [0033, 0038, 0046, 0061-0063]). Chazan et al. also teach wherein the microfluidic channels and passages have a depth and width of 0.1 μm and 500 μm (see [0071]).

Therefor it would have been obvious to one of skill in the art at the time of the invention to immobilize the nucleic acids directly to the support as taught by Fixe et al. and to utilize a microfluidic device as taught by Yamagata et al. and Chazan et al. in the method of analyzing samples taught by Elkins.

One would have been motivated to do so because Fixe et al. teach the stability of the covalent binding of the nucleic acids to the support and discuss the new possibilities for developing specialized systems (see p 8, col 2, paras1-2), and Yamagata et al and Chazan et al. teach the benefits of microfluidic devices, such as the ability to recover compounds that bind within the channels (see Yamagata et al. [0007]) and the ability to conduct high-throughput assays and to perform multiple reactions simultaneously in parallel, and the ability to precisely control temperature for biological reactions such as PCR and single nucleotide polymorphism genotyping (see Chazan et al. [0006-0007).

One would have had a reasonable expectation for success because Fixe et al. teach successfully immobilizing nucleic acids directly to the support and that the resulting bond was heat stable, Yamagata et al. and Chazan et al. teach successfully manufacturing microfluidic devices for biological assays such as PCR and single nucleotide polymorphism genotyping, and Elkins teaches successfully assaying samples by utilizing nucleic acid capture agents.

Therefor the teachings of Elkins, Fixe et al., Yamagata et al., and Chazan et al. renders the present invention prima facie obvious.

In addition, it would have been obvious to one skilled in the art to substitute one known element (i.e.: binding the nucleic acid directly to the support taught by Fixe et al. and a microfluidic device as the support as taught by Chazan et al. and Yamagata et al.) for another known element (i.e.: binding through a biotin linkage and array support taught by Elkins) using known methods (i.e.: the methods taught by all the cited references) with no change in their respective functions, and the substitution would have yielded the predictable results of a microfluidic device comprising nucleic acids bound directly to the substrate to one of ordinary skill in the art at the time of the invention. See KSR International Co. v. Teleflex Inc., USPQ2d 1385 (U.S. 2007).

Common Ownership of Claimed Invention Presumed

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. §§ 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Conclusions

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHANNON JANSSEN whose telephone number is (571)270-1303. The examiner can normally be reached on Monday-Friday 10:00AM-7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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